

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule encoding a *Renilla reniformis* green fluorescent protein, comprising a sequence of nucleotides that encodes the protein of SEQ ID No. 27 or a green fluorescent protein encoded by a *Renilla reniformis* having at least 80% sequence identity thereto.
2. An isolated nucleic acid molecule of claim 1 that encodes a protein having at least 90% sequence identity to the protein of SEQ ID No. 27.
3. The isolated nucleic acid molecule of claim 1, comprising a sequence of nucleotides selected from the group consisting of:
 - (a) the coding portion of the sequence of nucleotides set forth in any of SEQ ID Nos. 23-25;
 - (b) a sequence of nucleotides that hybridizes under high stringency to the sequence of nucleotides of (a); and
 - (c) a sequence of nucleotides comprising degenerate codons of (a) or (b).
4. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid is DNA.
5. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid is RNA.
6. A nucleic acid probe or primer, comprising at least 14 contiguous nucleotides selected from the sequence of nucleotides set of claim 1.
7. The probe or primer of claim 6, comprising at least 16 contiguous nucleotides selected from the sequence of nucleotides in claim 1.
8. The probe or primer of claim 7, comprising at least 30 contiguous nucleotides.
9. A plasmid, comprising the sequence of nucleotides of claim 1.

10. The plasmid of claim 8 that is an expression vector,
comprising:

- a promoter element;
- a cloning site for the introduction of nucleic acid; and
- 5 a selectable marker;

wherein the nucleic acid encoding the cloning site is positioned between nucleic acids encoding the promoter element and the green fluorescent protein and wherein the nucleic acid encoding the green fluorescent protein is operatively linked to the promoter element.

10 11. The plasmid of claim 9, further comprising a sequence of nucleotides encoding a luciferase.

12. A recombinant host cell, comprising the plasmid of claim 9.

13. The cell of claim 12, wherein the cell is selected from the group consisting of a bacterial cell, a yeast cell, a fungal cell, a plant cell,
15 an insect cell and an animal cell.

14. An isolated substantially purified *Renilla reniformis* green fluorescent protein (GFP) encoded by the nucleic acid molecule of claim 1.

15. A mutein of the GFP of claim 14 that exhibits altered spectral properties.

20 16. A mutein of the GFP of claim 14 that exhibits a reduced tendency to form multimers.

17. A composition, comprising the green fluorescent protein of claim 14 and at least one component of a bioluminescence generating system.

25 18. The composition of claim 17, wherein the bioluminescence generating system is selected from those isolated from: an insect system, a coelenterate system, a ctenophore system, a bacterial system, a mollusk system, a crustacea system, a fish system, an annelid system, and an earthworm system.

30 19. The composition of claim 17, wherein the bioluminescence generating system is selected from those isolated from: fireflies,

Mnemiopsis, *Beroe ovata*, *Aequorea*, *Obelia*, *Vargula*, *Pelagia*, *Renilla*,
Pholas Aristostomias, *Pachystomias*, *Porichthys*, *Cypridina*, *Aristostomias*,
 such *Pachystomias*, *Malacosteus*, *Gonadostomias*, *Gaussia*, *Watensia*,
Halisturia, Vampire squid, *Glyphus*, Mycotophids, *Vinciguerria*, *Howella*,
 5 *Florenciella*, *Chaudiodus*, *Melanocostus*, Sea Pens, *Chroteuthis*,
Eucleoteuthis, *Onychoteuthis*, *Watasenia*, cuttlefish, *Sepiolina*,
Oplophorus, *Acanthophyra*, *Sergestes*, *Gnathophausia*, *Argyropelecus*,
Yarella, *Diaphus*, *Gonadostomias* and *Neoscopelus*.

20. A mutein of claim 15, comprising substitution in amino acids
 10 at amino acids 56-75 of SEQ ID No. 27, whereby spectral properties are
 altered.

21. The composition of claim 20, wherein the bioluminescence
 generating system is selected from those isolated from *Aequorea*, *Obelia*,
Vargula and *Renilla*.

15 22. A reporter gene construct, comprising the nucleic acid of
claim 1.

23. A combination, comprising:
 an article of manufacture; and
 a *Renilla reniformis* green fluorescent protein (GFP) encoded
 20 by a nucleic acid molecule of claim 1.

24. The combination of claim 23, further comprising
 at least one component of a bioluminescence generating
 system, whereby the combination is a novelty item.

25 25. The combination of claim 24, wherein the component of the
 bioluminescence generating system comprises a luciferase.

26. The combination of claim 24, wherein the component of the
 bioluminescence generating system comprises a luciferin.

27. The combination of claim 23, wherein the article of
 manufacture is selected from among toys, fountains, personal care items,
 30 fairy dust, foods, textile and paper products.

28. The combination of claim 27, wherein the article of manufacture is selected from among toy guns, pellet guns, greeting cards, fingerpaints, foot bags, slimy play material, clothing, bubble making toys and bubbles therefor, balloons, bath powders, body lotions, gels, body powders, body creams, toothpastes, mouthwashes, soaps, body paints, bubble bath, board game toys, fishing lures, egg-shaped toys, toy cigarettes, dolls, sparklers, magic wand toys, wrapping paper, gelatins, icings, frostings, fairy dust, beer, ornamental transgenic plants, wine, champagne, milk, soft drinks, ice cubes, ice, dry ice, soaps, body paints and bubble bath.

29. The combination of claim 28 that is a transgenic ornamental plant.

30. The combination of claim 28 that is a toy.

31. The combination of claim 28 that is a food.

32. The combination of claim 28 that is a cosmetic.

33. The combination of claim 28 that is a beverage.

34. The combination of claim 24, wherein the article of manufacture is selected from among toys, fountains, personal care items, fairy dust, foods, textile, transgenic ornamental plant and paper products.

35. The combination of claim 34, wherein the article of manufacture is selected from among toy guns, pellet guns, greeting cards, fingerpaints, foot bags, slimy play material, clothing, bubble making toys and bubbles therefor, balloons, bath powders, body lotions, gels, body powders, body creams, toothpastes, mouthwashes, soaps, body paints, bubble bath, board game toys, fishing lures, egg-shaped toys, toy cigarettes, dolls, sparklers, magic wand toys, wrapping paper, gelatins, icings, frostings, fairy dust, beer, wine, champagne, soft drinks, ice cubes, ice, dry ice, soaps, body paints and bubble bath.

36. An antibody that specifically binds to *Renilla reniformis* or a molecule or derivative of the antibody containing the binding domain thereof.

37 The antibody of claim 36 that is a monoclonal antibody.

38. A nucleic acid construct, comprising a nucleotide sequence encoding a luciferase and a sequence of nucleotides of claim 1 that encodes a *Renilla reniformis* fluorescent protein (GFP).

5 39. The nucleic acid construct of claim 38, wherein the luciferase is a *Renilla mulleri* luciferase, a *Gaussia* luciferase or a *Pleuromamma* luciferase.

40. The nucleic acid construct of claim 39, wherein the *Gaussia* luciferase is a *Gaussia princeps* luciferase.

10 41. The nucleic acid construct of claim 38, wherein the luciferase is encoded by:

a sequence of nucleotides set forth in SEQ ID No. 17, SEQ ID No. 19, or SEQ ID No. 28;

15 a sequence of nucleotides encoding the amino acid sequence set forth in SEQ ID No. 18, SEQ ID No. 20 or SEQ ID No. 29; and

a sequence of nucleotides that hybridizes under high stringency to the sequence of nucleotides set forth in SEQ ID No. 17, SEQ ID No. 19 or SEQ ID No. 28.

42. The nucleic acid construct of claim 38 that is DNA.

20 43. The nucleic acid construct of claim 38 that is RNA.

44. A plasmid, comprising the nucleic acid construct of claim 38.

45. The plasmid of claim 44, further comprising a sequence of nucleotides encoding:

a promoter element;

25 a selectable marker;

wherein, the sequence of nucleotides encoding the luciferase and GFP is operatively linked to the promoter element, whereby the luciferase and GFP are expressed.

30 46. The construct of claim 38, wherein the luciferase and the GFP are encoded by a polycistronic message.

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47. The construct of claim 38, wherein the encoded luciferase and comprise a fusion protein.

48. The construct of claim 38, wherein the luciferase is *Renilla reniformis* luciferase.

5 49. A recombinant host cell, comprising the plasmid of claim 44.

50. The cell of claim 46, wherein the cell is selected from the group consisting of a bacterial cell, a yeast cell, a fungal cell, a plant cell, an insect cell and an animal cell.

10 51. An isolated substantially purified luciferase and GFP fusion protein, wherein the GFP is a *Renilla reniformis* GFP and the fusion protein is encoded by the nucleic acid construct of claim 47.

52. The fusion protein of claim 51, wherein the luciferase is a *Renilla* luciferase.

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15 53. The fusion protein of claim 51, wherein the luciferase and is a *Renilla reniformis* luciferase.

54. A composition, comprising the fusion protein of claim 48.

55. The composition of claim 54, further comprising at least one component of a bioluminescence generating system.

20 56. The composition of claim 55, wherein the component of the bioluminescence generating system is a luciferin.

57. The nucleic acid construct of claim 47, wherein the sequence of nucleotides encoding the luciferase and GFP are not contiguous.

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25 58. The nucleic acid construct of claim 54, comprising a sequence of nucleotides that encodes a ligand binding domain of a target protein.

59. A biosensor, comprising a GFP protein encoded by the nucleic acid molecule of claim 1 and a luciferase.

30 60. The biosensor of claim 59, wherein the luciferase is a *Renilla* luciferase.

61. A biosensor of claim 59, further comprising a modulator.

62. A biosensor, comprising a fusion protein of claim 51.

63. The biosensor of claim 62, wherein the GFP and luciferase in the fusion protein are not contiguous.

64. A bioluminescence resonance energy transfer (BRET) system, comprising:

(a) a GFP encoded by the nucleic molecule of claim 1;

(b) a luciferase from which the GFP can accept energy when the GFP and luciferase;

(c) a luciferin or other substrate of the luciferase.

65. The BRET system of claim 64, further comprising one or more modulators.

66. The BRET system of claim 65, wherein the GFP and luciferase are each attached to a different modulator, or each are attached to the same modulator.

67. The BRET system of claim 65, wherein a conformation change in a modulator causes an increase in the proximity of the luciferase and GFP.

68. The BRET system of claim 65, wherein a conformational change in a modulator causes a decrease in the proximity of the luciferase and GFP.

69. The BRET system of claim 65, wherein the luciferase is *Renilla reniformis* luciferase.

70. A microelectronic device, comprising:

a substrate;

a plurality of micro-locations defined on the substrate, wherein each micro-location is for linking a macromolecule;

an independent photodetector integrated at or adjacent to each micro-location and optically coupled to each micro-location, each photodetector being configured to generate a sensed signal responsive to the photons of light emitted at the corresponding micro-location when a light-emitting chemical reaction occurs at that micro-location, each

photodetector being independent from the photodetectors optically coupled to the other micro-locations; and

an electronic circuit coupled to each photodetector and configured to read the sensed signal generated by each photodetector and to generate output data signals therefrom that are indicative of the light emitted at each micro-location by the light-emitting chemical reactions, whereby the device detects photons of light emitted by light-emitting chemical reactions, wherein:

each micro-location is defined by a portion of the surface;

- 10 the micro-locations defined on the substrate each comprise a components of a bioluminescence generating system and a green fluorescent protein of claim 1, whereby photons of light are emitted when a reaction takes place at that micro-location

- 15 71. The device of claim 70, wherein the micro-locations are provided as an array.

72. The device of claim 70, wherein the bioluminescence generating system comprises a *Renilla* luciferase.

73. The device of claim 71, wherein the bioluminescence generating system comprises a *Renilla reniformis* luciferase.

- 20 74. A method of detecting and identifying analytes in a biological sample, comprising:

providing the microelectronic device of claim 70;

attaching a macromolecule or plurality of different macromolecules to the surface at each micro-location on the device, wherein

- 25 macromolecule is specific for binding to selected analyte that may be present in the biological sample;

contacting the sample with the surface of the microelectronic device, whereby any of the selected analytes that are present in the sample bind to the macromolecule attached to the surface at each micro-

- 30 location;

exposing the surface of the microelectronic device to a second macromolecule or plurality thereof bind to the selected analyte already bound to the first macromolecule at each micro-location, wherein the second macromolecule comprises a component of a bioluminescence generating reaction;

initiating the bioluminescence generating reaction by contacting the surface of the device with the remaining components of the bioluminescence generating reaction, wherein the wavelength of the resulting light is shifted by the *Renilla reniformis* GFP;

detecting photons of light emitted by the GFP using a photodetector optically coupled to each micro-location, each photodetector generating a sensed signal representative of the bioluminescence generation at the respective micro-location.

75. A transgenic animal or plant that expresses the *Renilla reniformis* nucleic acid of claim 1.

76. The transgenic animal or plant of claim 75, selected from among fish, worms, monkeys, rodents, goats, pigs, cows, sheep, horses, flowering plants, ornamental plants.

77. The transgenic animal or plant of claim 75 that is an orchid.